U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: BERCH Serial Number: US03/10/395,544

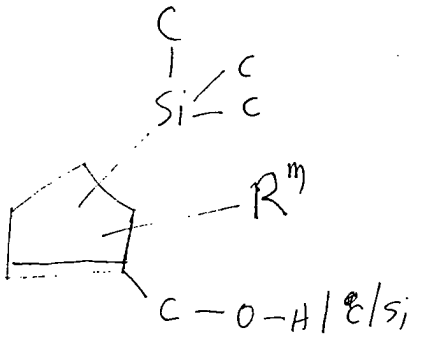
Date: 5/17/04 Phone: 571-272-0663 Art Unit: 1624

Office Rem 5C01 Mailbox 5C18

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

10/734,012



R^m = C(=O)-OH/C or C(A)(A')-C-(H/C)

A, A' = H / CH_3

Claim 25, 33, 40etc

#1 of 6

G/III

STAFF USE ONLY

Date completed: 8/9/04

Searcher: Arnold (rev. Schulwitz)

Terminal time: _____

Elapsed time: _____

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG

_____ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1580 (9-90)

Today

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

122179

SEARCH REQUEST FORM

Requestor's Name: BERCH

Serial Number: US03/39554F

Date: 5/17/04 Phone: 571-272-0663 Art Unit: 1624

Office Rem 5C01 Mailbox 5C18

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

10/734012

~~CAN~~ a entecavir

Synthesis or preparation

Claim

6 of 6

Sp II

STAFF USE ONLY

=> file reg; d rn cn l1
FILE 'REGISTRY' ENTERED AT 15:20:25 ON 19 MAY 2004

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 MAY 2004 HIGHEST RN 683203-75-0
DICTIONARY FILE UPDATES: 18 MAY 2004 HIGHEST RN 683203-75-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 142217-69-4 REGISTRY
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(1S,3R,4S)-4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]-, [1S-(1α,3α,4β)]-
OTHER NAMES:
CN BMS 200475
CN **Entecavir**
CN SQ 34676

=> => file caplus; d que l4
FILE 'CAPLUS' ENTERED AT 15:45:50 ON 19 MAY 2004

FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate

substance identification.

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L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENTECAVIR/CN
L2           50 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1
L3           56 SEA FILE=CAPLUS ABB=ON  PLU=ON  ENTECAVIR OR SQ 34676
L4            9 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L2 OR L3) (L) PREP/RL


=> file medline; d que l6
FILE 'MEDLINE' ENTERED AT 15:45:57 ON 19 MAY 2004

 FILE LAST UPDATED: 18 MAY 2004 (20040518/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L5           46 SEA FILE=MEDLINE ABB=ON  PLU=ON  ENTECAVIR OR SQ 34676
L6            0 SEA FILE=MEDLINE ABB=ON  PLU=ON  (SYNTH? OR PREP?) (10A) L5


=> file embase; d que l19

L12         157 SEA FILE=EMBASE ABB=ON  PLU=ON  ENTECAVIR/CT
L15      127175 SEA FILE=EMBASE ABB=ON  PLU=ON  DRUG SYNTHESIS/CT
L17          26 SEA FILE=EMBASE ABB=ON  PLU=ON  L12/MAJ
L18          12 SEA FILE=EMBASE ABB=ON  PLU=ON  L12 (L) DV/CT
L19           4 SEA FILE=EMBASE ABB=ON  PLU=ON  (L17 OR L18) AND L15


=> file biosis; d que l24
FILE 'BIOSIS' ENTERED AT 15:46:25 ON 19 MAY 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 May 2004 (20040512/ED)

FILE RELOADED: 19 October 2003.


L20          71 SEA FILE=BIOSIS ABB=ON  PLU=ON  ENTECAVIR
L21          29 SEA FILE=BIOSIS ABB=ON  PLU=ON  BMS200475 OR BMS 200475 OR
                SQ34676 OR SQ 34676
L22     3426655 SEA FILE=BIOSIS ABB=ON  PLU=ON  SYNTH? OR PREP? OR DEVELOP?
L23          20 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L20 OR L21) AND L22
L24           5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L23 AND (CARBOCYCLIC OR
                SYNTHESIS)/TI
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=> file wpid; d que l29
FILE 'WPIDS' ENTERED AT 15:46:31 ON 19 MAY 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED:          14 MAY 2004      <20040514/UP>
MOST RECENT DERWENT UPDATE:     200431        <200431/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/           <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/               <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
    FIRST VIEW - FILE WPIFV. FREE CONNECT HOUR UNTIL 1 MAY 2004.
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>>> NEW! IMPROVE YOUR LITIGATION CHECKING AND INFRINGEMENT
    MONITORING WITH LITALERT. FIRST ACCESS TO RECORDS OF IP
    LAWSUITS FILED IN THE 94 US DISTRICT COURTS SINCE 1973.
    FOR FURTHER DETAILS:
    http://www.thomsonscientific.com/litalert           <<<

>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE
    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<

>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
    THERE WAS NO WEEKLY SDI RUN  <<<


L25           16 SEA FILE=WPIX ABB=ON  PLU=ON  ENTECAVIR OR BMS200475 OR BMS
                 (W) (200475 OR 200 475) OR SQ34676 OR SQ (W) (34676 OR 346 76)
L26      1773063 SEA FILE=WPIX ABB=ON  PLU=ON  PREP? OR SYNTH? OR DEVELOP? OR
                 ANALO? OR DERIV?
L29            2 SEA FILE=WPIX ABB=ON  PLU=ON  L25 (5A) L26


=> dup rem l4 l19 l24 l29
FILE 'CAPLUS' ENTERED AT 15:46:47 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 15:46:47 ON 19 MAY 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:46:47 ON 19 MAY 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)
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FILE 'WPIX' ENTERED AT 15:46:47 ON 19 MAY 2004
COPYRIGHT (C) 2004 THOMSON DERWENT
PROCESSING COMPLETED FOR L4
PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L24
PROCESSING COMPLETED FOR L29
L30          14 DUP REM L4 L19 L24 L29 (6 DUPLICATES REMOVED)
                ANSWERS '1-9' FROM FILE CAPLUS
                ANSWER '10' FROM FILE EMBASE
                ANSWERS '11-12' FROM FILE BIOSIS
                ANSWERS '13-14' FROM FILE WPIX

=> d ibib ab ed l30 1-12; d ibib ab ed abex l30 13-14

L30  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:        2003:1001880  CAPLUS
DOCUMENT NUMBER:         140:235989
TITLE:                   Novel 3'-deoxy analogs of the anti-HBV agent
                         entecavir: synthesis of enantiomers from a single
                         chiral epoxide
AUTHOR(S):               Ruediger, Edward; Martel, Alain; Meanwell, Nicholas;
                         Solomon, Carola; Turmel, Brigitte
CORPORATE SOURCE:        Bristol-Myers Squibb Pharmaceutical Research
                         Institute, Candiac, QC, J5R 1J1, Can.
SOURCE:                  Tetrahedron Letters (2004), 45(4), 739-742
                         CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   A synthesis of novel 3'-deoxy analogs of the anti-HBV agent entecavir
     (BMS-200475) was devised using regioselective ring opening of suitable
     cyclopentene epoxides as the key step.  This versatile approach afforded
     access to an enantiomeric pair of carbocyclic nucleosides from a single
     chiral intermediate.  Contrary to the potent anti-HBV activity shown by
     entecavir, the synthesized 3'-deoxy analogs proved to be inactive against
     HBV.
ED   Entered STN:  24 Dec 2003
REFERENCE COUNT:         29    THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30  ANSWER 2 OF 14  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER:        2003:827762  CAPLUS
DOCUMENT NUMBER:         140:42353
TITLE:                   Radical cyclization studies directed toward the
                         synthesis of BMS-200475 'entecavir': the carbocyclic
                         core
AUTHOR(S):               Ziegler, Frederick E.; Sarpong, Martha A.
CORPORATE SOURCE:        Sterling Chemistry Laboratory, Yale University, New
                         Haven, CT, 06520-8107, USA
SOURCE:                  Tetrahedron (2003), 59(45), 9013-9018
                         CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Two routes are presented for the conversion of D-diacetone glucose into a
     protected carbocyclic core of BMS-200475 (Entecavir) I.  The reduction of two
     terminal epoxides with Cp2TiCl to form carbon radicals and their
     cyclizations with a terminal acetylene and an α,β-unsatd. ester
     lead ultimately to an allylic alc., a candidate for Mitsunobu coupling
     with guanine.
```

ED Entered STN: 22 Oct 2003
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2001:438052 CAPLUS
DOCUMENT NUMBER: 136:193422
TITLE: Entecavir; Bristol-Myers Squibb
AUTHOR(S): Billich, Andreas
CORPORATE SOURCE: General Dermatology, Novartis Research Institute, Vienna, A-1235, Austria
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(5), 617-621
CODEN: COIDAZ
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Bristol-Myers Squibb is developing entecavir, a viral replication inhibitor, for the potential treatment of hepatitis B virus (HBV) infection. The compound is a cyclopentylguanosine analog and is in phase II trials in the US. Entecavir was originally developed as SQ-34676 for the treatment of herpes simplex virus infections but displayed only moderate activity, which eventually led to discontinuation of development for this indication. However, Bristol-Myers Squibb later discovered that entecavir was extremely potent against HBV (ED50 = 3.0 nM, compared with 200 nM for lamivudine) with relatively low toxicity and acting through inhibition of DNA polymerase. The triphosphate form is a potent HBV polymerase inhibitor in both woodchuck and duck models. By Sept. 2000, a large-scale clin. trial was underway in China for HBV infection and by Oct. 2000 phase I trials were ongoing in Japan.
ED Entered STN: 18 Jun 2001
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1997:123302 CAPLUS
DOCUMENT NUMBER: 126:225503
TITLE: BMS-200475, a novel carbocyclic 2'-deoxyguanosine analog with potent and selective anti-hepatitis B virus activity in vitro
AUTHOR(S): Bisacchi, G. S.; Chao, S. T.; Bachard, C.; Daris, J. P.; Innaimo, S.; Jacobs, G. A.; Kocy, O.; Lapointe, P.; Martel, A.; et al.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(2), 127-132
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:225503
AB BMS-200475, a novel carbocyclic analog I of 2'-deoxyguanosine, is a potent inhibitor of hepatitis B virus in vitro (ED50 = 3 nM) with relatively low cytotoxicity (CC50 = 21-120 μM). A practical 10-step asym. synthesis was developed affording BMS-200475 in 18% overall chemical yield and >99% optical purity. The enantiomer of BMS-200475 as well as the adenine, thymine, and iodouracil analogs are much less active.
ED Entered STN: 22 Feb 1997
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:547519 CAPLUS
DOCUMENT NUMBER: 139:197702
TITLE: Radical cyclization studies in the 5-exo mode: application toward the synthesis of bms-200475
AUTHOR(S): Sarpong, Martha Abena Afraso
CORPORATE SOURCE: Yale Univ., New Haven, CT, USA
SOURCE: (2002) 367 pp. Avail.: UMI, Order No. DA3068346 From: Diss. Abstr. Int., B 2003, 63(10), 4685
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
ED Entered STN: 17 Jul 2003

L30 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:174761 CAPLUS
DOCUMENT NUMBER: 137:365822
TITLE: Synthesis of tritiated entecavir ([3H]BMS-200475), a novel carbocyclic 2'-deoxyguanosine analog
AUTHOR(S): Rinehart, J. K.; Egli, P.; Bisacchi, G. S.; Merchant, Z.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001), Meeting Date 2000, 155-158. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Entecavir (BMS-200475) and recently-marketed lamivudine are examples of new nucleoside analogs that can control hepatitis B virus (HBV) replication. A tritiated analog of BMS-200475 was used for biol. studies since the mol. contains an exocyclic double bond. Oxidation of the 3'-hydroxymethyl group of the parent BMS-200475 to the aldehyde and subsequent reduction with sodium boro[3H]hydride appeared to be the most efficient pathway to the desired product. A protection-deprotection scheme for entecavir (BMS-200475) was develop to allow the oxidation of the hydroxymethyl group to an aldehyde in the presence of an exocyclic double bond. The protected aldehyde was reduced with sodium boro[3H]hydride, the product was subjected to stepwise deprotection and the crude product was purified by preparative high performance liquid chromatog. to yield 98.4% pure [3H]BMS-200475 (13.9 Ci/mmol, 514 MBq/mmol). [3H]BMS-200475 was prepared in three radiochem. steps from the aldehyde in an overall 26% radiochem. yield.
ED Entered STN: 11 Mar 2002
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:529169 CAPLUS
DOCUMENT NUMBER: 131:170633
TITLE: Preparation of amino acid-containing prodrugs
INVENTOR(S): Johansson, Nils Gunnar; Zhou, Xiao-xiong; Wahling, Horst; Sund, Christian; Wallberg, Hans; Salvador, Lourdes; Lindstrom, Stefan

PATENT ASSIGNEE(S): Medivir AB, Swed.
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941275	A1	19990819	WO 1999-SE194	19990215
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9807267	A	19990215	ZA 1998-7267	19980813
WO 9909031	A1	19990225	WO 1998-SE1467	19980814
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1123935	A2	20010816	EP 2001-103370	19980814
EP 1123935	A3	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
NZ 508502	A	20020426	NZ 1998-508502	19980814
ZA 9901148	A	19990812	ZA 1999-1148	19990212
CA 2318978	AA	19990819	CA 1999-2318978	19990215
AU 9932820	A1	19990830	AU 1999-32820	19990215
AU 754733	B2	20021121		
EP 1054891	A1	20001129	EP 1999-932500	19990215
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CA 2325523	AA	19991014	CA 1999-2325523	19990330
WO 9951613	A1	19991014	WO 1999-SE528	19990330
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1121366	A1	20010808	EP 1999-921327	19990330
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002510698	T2	20020409	JP 2000-542334	19990330
WO 2000047561	A1	20000817	WO 1999-SE1403	19990818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG,				

MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9956658	A1	20000829	AU 1999-56658	19990818
AU 770801	B2	20040304		
EP 1150956	A1	20011107	EP 1999-943591	19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536435	T2	20021029	JP 2000-598482	19990818
US 2002128301	A1	20020912	US 2001-927254	20010810

PRIORITY APPLN. INFO.:

SE 1998-452	A	19980213
SE 1998-469	A	19980216
SE 1998-1216	A	19980403
ZA 1998-7267	A	19980813
WO 1998-SE1467	W	19980814
SE 1998-3438	A	19981007
SE 1997-2957	A	19970815
SE 1997-4147	A	19971112
EP 1998-939041	A3	19980814
NZ 1998-502837	A1	19980814
US 1999-249317	A	19990212
WO 1999-SE194	W	19990215
WO 1999-SE528	W	19990330
WO 1999-SE1403	W	19990818

OTHER SOURCE(S): MARPAT 131:170633

AB Pharmaceutical compds. or intermediates in their synthesis D*-Linker*(R2')k-R2 [R2 and R2' (if present) is the amide or ester residue of an aliphatic amino acid, k is 0 or 1, D* is a drug residue bearing an accessible function selected from amine, hydroxy and carboxy, or a group amenable to attachment to the accessible function, Linker* is an at least bifunctional linker comprising a first function bound to the accessible function spaced from a second function forming an amide or acyl bond with the aliphatic amino acid] were prepared Thus, 2',3'-dideoxy-3'-fluoro-5'-O-{3-[1,3-bis(L-valyloxy)-2-propyloxycarbonyl]propanoyl}guanosine was prepared and shown to provide significantly enhanced oral bioavailability relative to the active metabolite 2',3'-dideoxy-3'-fluoroguanosine.

ED Entered STN: 24 Aug 1999
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:175923 CAPLUS
DOCUMENT NUMBER: 128:244287
TITLE: Improved process for preparing the antiviral agent [1S-(1α,3α,4β)]-2-amino-1,9-dihydro-9-[4-hydroxy-3-(hydroxymethyl)-2-methylene-cyclopentyl]-6h-purin-6-one
INVENTOR(S): Bisacchi, Gregory S.; Sundeen, Joseph E.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9809964	A1	19980312	WO 1997-US15007	19970826
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9740906	A1	19980326	AU 1997-40906	19970826

PRIORITY APPLN. INFO.: US 1996-25378P P 19960903
WO 1997-US15007 W 19970826

OTHER SOURCE(S): CASREACT 128:244287; MARPAT 128:244287

AB Improvements in the yield of the antiviral agent cyclopentylpurinone carbocyclic nucleosides I (R = trityl protecting group; R1R2 = O) are obtained by employing Dess-Martin periodinane to convert the cyclopentol I (R = trityl protecting group; R1 = H, R2 = OH) and the methylenation of this cyclopentanone by use of a Nysted reagent, Tebbe reagent, or a reagent prepared from zinc powder, diiodomethane, lead powder or lead chloride, and titanium tetrachloride in a suitable solvent. Thus, [1S-(1α,3α,4β)]-2-amino-1,9-dihydro-9-[4-hydroxy-3-(hydroxymethyl)-2-methylene-cyclopentyl]-6H-purin-6-one monohydrate was prepared via Dess-Martin periodinane oxidation and methylenation of this cyclopentanone by use of a Nysted reagent, Tebbe reagent.

ED Entered STN: 25 Mar 1998

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1992:449162 CAPLUS
DOCUMENT NUMBER: 117:49162
TITLE: Preparation of [hydroxymethyl (methylenecyclopentyl)]purines and pyrimidines as virucides
INVENTOR(S): Zahler, Robert; Slusarchyk, William A.
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 481754	A2	19920422	EP 1991-309525	19911016
EP 481754	A3	19920916		
EP 481754	B1	19970820		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5206244	A	19930427	US 1991-763033	19910920
ZA 9107894	A	19930331	ZA 1991-7894	19911002
AU 9185598	A1	19920430	AU 1991-85598	19911004
AU 634423	B2	19930218		
CA 2053339	AA	19920419	CA 1991-2053339	19911011
CA 2053339	C	20010529		
IL 99755	A1	19960804	IL 1991-99755	19911015
AT 157095	E	19970915	AT 1991-309525	19911016
ES 2104673	T3	19971016	ES 1991-309525	19911016
SG 70958	A1	20000321	SG 1996-2080	19911016

NO 9104089	A	19920421	NO 1991-4089	19911017
NO 179906	B	19960930		
NO 179906	C	19970108		
HU 59109	A2	19920428	HU 1991-3283	19911017
HU 213207	B	19970328		
RU 2037496	C1	19950619	RU 1991-5001946	19911017
FI 9104928	A	19920419	FI 1991-4928	19911018
CN 1061972	A	19920617	CN 1991-110831	19911018
CN 1030916	B	19960207		
JP 04282373	A2	19921007	JP 1991-271121	19911018
JP 2994117	B2	19991227		
PL 169403	B1	19960731	PL 1991-292101	19911018
US 5340816	A	19940823	US 1993-4006	19930115

PRIORITY APPLN. INFO.: US 1990-599568 A 19901018
US 1991-763033 A3 19910920

OTHER SOURCE(S): MARPAT 117:49162

AB Title compds. [I; R1 = Q1-Q3, etc.; R2 = F, Cl, Br, iodo, H, Me, CF3, Et, Pr, FCH2CH2, ClCH2CH2, HC.tplbond.C, trans-HC:CHR3; R3 = Cl, Br, iodo, H, Me, CF3; R6, R7 = H, PO3H2, COR5; R5 = H, aryl, (substituted) alkyl], were prepared Thus, [1(S)-[1α(E),2β,3α,4β]]-3-[1,2,3,4-tetrahydro-1-[2-hydroxy-4-(phenylmethoxy)-3-[(phenylmethoxy)methyl]cyclopentyl]-2,4-dioxo-5-pyrimidinyl]-2-propenoic acid (preparation starting from cyclopentadiene, PhCH2OCH2Cl, and (-)-diisopinocampheylborane given) was stirred 17 h with KHCO3 and N-chlorosuccinimide in DMF to give a (E)-chloroethenylpyrimidine derivative, which was oxidized to the cyclopentanone with DCC/Me2SO. This was methylenated with Zn/TiCl4/CH2Br2 in THF and the product was deprotected with BCl3 in CH2Cl2 at -78° to give title compound II. II inhibited Herpes simplex type 1 schooler strain in MT-2 cells with ID50 = 0.07-0.16 μM.

ED Entered STN: 08 Aug 1992

L30 ANSWER 10 OF 14 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003087897 EMBASE
TITLE: ACH-126443. Anti-HBV, anti-HIV.
AUTHOR: Sorbera L.A.; Castaner J.; Bayes M.
CORPORATE SOURCE: L.A. Sorbera, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
SOURCE: Drugs of the Future, (1 Dec 2002) 27/12 (1131-1140).
Refs: 26
ISSN: 0377-8282 CODEN: DRFUD4
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Chronic hepatitis B virus (HBV) infection is a major global health concern with an estimated 1-2 million individuals dying every year from hepatitis B-related disease. The goal of treatment for chronic HBV infection is to suppress HBV replication prior to development of irreversible liver damage which ideally would be accomplished with antiviral agents and immunomodulatory therapy. Over the past 10 years, research has focused on the development of anti-HBV agents able to directly block HBV replication. Naturally occurring nucleoside analogues were used early to treat hepatitis B with little success or high levels of toxicity. The search for novel nucleoside-based chemotherapies continues through modification of the naturally occurring nucleoside-based agents. Of the new generation

nucleoside analogues, lamivudine proved to be a potent and well tolerated inhibitor of HBV replication and is clinically available for the treatment of chronic HBV infection. However, long-term treatment with the agent is associated with the development of drug resistance. ACH-126443 is a novel unnatural L-nucleoside reverse transcriptase inhibitor that has shown potent and selective activity against HBV and has also shown significant efficacy against HIV. Due to its promising potent preclinical profile, ACH-126443 was selected for further development as a treatment for chronic HBV and HIV infections.

L30 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:147519 BIOSIS
DOCUMENT NUMBER: PREV200300147519
TITLE: Rapid **synthesis** of (+-)-r-7-benzyloxymethyl-cyclopenta-cis-(4,5)(1,3)-oxazolo(3,2-a)pyrimidinones versatile **carbocyclic** nucleoside precursors.
AUTHOR(S): Perez, Nury; Gordillo, Barbara [Reprint Author]
CORPORATE SOURCE: Departamento de Quimica, Centro de Investigacion y de Estudios Avanzados del Instituto Politecnico Nacional, 07000, Apartado Postal 14-740, Mexico City, DF, Mexico ggordill@mail.cinvestav.mx
SOURCE: Tetrahedron, (27 January 2003) Vol. 59, No. 5, pp. 671-676. print.
ISSN: 0040-4020 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003
AB (+-)-r-7-Benzyloxymethyl-cyclopenta-cis-(4,5)(1,3)-oxazolo(3,2-a)pyrimidinones were **synthesized** in two steps from 1-hydroxymethyl-3-cyclopentene. These compounds are versatile intermediates for the **synthesis** of carbocyclic nucleosides. The **synthesis** has been accomplished by the iodofunctionalization of olefins as a method of coupling the pyrimidine bases and the carbocycle.
ED Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003

L30 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:267727 BIOSIS
DOCUMENT NUMBER: PREV200200267727
TITLE: **Synthesis** of novel (2R,4R)- and (2S,4S)-iso dideoxynucleosides with exocyclic methylene as potential antiviral agents.
AUTHOR(S): Yoo, Su Jeong; Kim, Hea Ok; Lim, Yoongho; Kim, Jeongmin; Jeong, Lak Shin [Reprint author]
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, College of Pharmacy, Ewha Womans University, Seoul, 120-750, South Korea lakjeong@mm.ewha.ac.kr
SOURCE: Bioorganic and Medicinal Chemistry, (January, 2002) Vol. 10, No. 1, pp. 215-226. print.
ISSN: 0968-0896.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002
AB Novel (2R,4R)- and (2S,4S)-iso dideoxynucleosides with exocyclic methylene have been designed and **synthesized**, based on the lead **BMS-200475** (3) which exhibited potent anti-HBV activity. For the **synthesis** of D types of (2R,4R)-nucleosides, L-xylose was converted to the key intermediate 14. The intermediate 14 was

converted to the uracil derivative 4a and the cytosine derivative 4b. Compound 14 was also converted to the purine derivatives such as adenine derivative 4c, hypoxanthine derivative 4d, and guanine derivative 4e. The corresponding L types of (2S,4S)-enantiomers were more efficiently **synthesized** from the commercially available 1,2-isopropylidene-D-xylose (20) than the **synthetic** method used in the **synthesis** of (2R,4R)-nucleosides. The key intermediate 25 was converted to the pyrimidine analogues 5a and 5b and the purine derivatives 5c, 5d, and 5e using the similar method used in the **preparation** of 4c, 4d, and 4e. The **synthesized** final (2R,4R)- and (2S,4S)-nucleosides were tested against several viruses such as HIV-1, HSV-1, HSV-2, HCMV and HBV. (2R,4R)-Adenine analogue 4c exhibited potent anti-HBV activity (EC50 = 1.5 muM in 2.2.15 cells) among compounds tested, while (2R,4R)-uracil derivative 4a was the most active against HCMV among compounds tested and (2R,4R)-adenine derivative 4c was found to be moderately active against the same virus. However, the corresponding (2S,4S)-isomers were found to be totally inactive against all tested viruses. Both (2R,4R)-adenine derivative 4c and (2S,4S)-adenine analogue 5c were totally resistant to the adenosine deaminase like iso-ddA (1). From the molecular modeling study the hydroxymethyl side chains of **BMS-200475** (3) and 4c were almost overlapped, indicating that 4c may be suitable for phosphorylation by cellular kinases like the lead 3, but some discrepancy between two bases was observed, indicating why 4c is less potent against HBV than 3. It is concluded that discovery of (2R,4R)-adenine analogue 4c as potent anti-HBV agent suggested that the sugar moiety of this series can be regarded as a novel template for the **development** of new anti-HBV agent and oxygen atom can be acted as a bioisostere of C-OH.

ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002

L30 ANSWER 13 OF 14 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-119235 [12] WPIX
DOC. NO. CPI: C2004-047948
TITLE: Liquid composition useful for treating hepatitis B virus infection comprises solvent and entecavir in a low dose.
DERWENT CLASS: A96 B02 B05 B07
INVENTOR(S): DESAI, D; LI, D
PATENT ASSIGNEE(S): (DESA-I) DESAI D; (LIDD-I) LI D; (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003190334	A1	20031009	(200412)*		8
WO 2003086367	A1	20031023	(200412)	EN	

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003190334	A1 Provisional	US 2002-370674P	20020408
		US 2003-407287	20030404
WO 2003086367	A1	WO 2003-US10371	20030403

PRIORITY APPLN. INFO: US 2002-370674P 20020408; US 2003-407287 20030404

AB US2003190334 A UPAB: 20040218
NOVELTY - A liquid composition (C1) comprises solvent and entecavir 0.001 - 20, (preferably 0.02) w/v.%.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a powder (P1) for constitution at the time of use as a liquid pharmaceutical composition comprising entecavir 0.001 - 20, (preferably 0.11) w/v.%;

(2) **preparation** of oral composition comprising dissolving **entecavir** 0.001 - 20 w/v. % and preservative in a solution comprising solvent; and

(3) preparation of a powder for reconstitution at the time of use as a liquid pharmaceutical composition for oral administration comprising mixing entecavir (0.001 - 20 weight %) with at least one additional component selected from sweetener, preservative, flavoring agent and/or buffering agent.

ACTIVITY - Hepatotropic; Virucide; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - For treating hepatitis B virus infection (claimed)

ADVANTAGE - (C1) is capable of safely and effectively treating hepatitis B virus infection; is ready-to-use; is both stable and palatable; can be formulated from a powder for constitution as a liquid composition at the time of use.

Dwg.0/0

ED 20040218

ABEX UPTX: 20040218
ADMINISTRATION - (C1) is administered orally (claimed).
No dosage given.

EXAMPLE - A liquid composition (0.2 mg/ml) was prepared using the following ingredients: (g/100 ml) entecavir (0.02), Lycasin (RTM; maltitol) as sweetener (65), methylparaben as preservative (0.2), propylparaben as preservative (0.028), cherry/guarana/orange as flavoring agent (0.05/0.025/0.025), citric acid/sodium citrate as buffering agent (0.96/1.47 for (100 mM) or 0.037/0.24 for (10 mM)) and water as solvent (q.s to 100 ml pH 6). The composition was ready-to-use and the potency of entecavir, methylparaben and propylparaben was 0.204, 1.87 and 0.264 initially; 0.201, 1.96 and 0.277 after 4 days at 25 degreesC/HIL/UVA, PROT; 0.203, 1.99 and 0.282 after 2 weeks at 25 degreesC/HIL/UVA, PROT; 0.205, 1.97 and 0.280 after 4 weeks at 30 degreesC/60% relative humidity; 0.205, 2.09 and 0.299 after 13 weeks at 25 degreesC/60% relative humidity; and 0.206, 1.99 and 0.284 after 26 weeks at 5 degreesC respectively. Thus the composition was extremely stable over an extended period of time at varying temperatures.

L30 ANSWER 14 OF 14 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-335678 [35] WPIX
DOC. NO. CPI: C2001-103672
TITLE: Use of lamivudine and BMS-200475 to treat hepatitis B virus infection resistant to nucleoside and/or non-nucleoside inhibitors of HBV replication, may potentially provide synergistic antiviral effects.

DERWENT CLASS: B03
INVENTOR(S): BROWN, N A; CONDREAY, L D; GRAY, D F; RUBIN, M
PATENT ASSIGNEE(S): (GLAX) GLAXO GROUP LTD; (BROW-I) BROWN N A; (COND-I) CONDREAY L D; (GRAY-I) GRAY D F; (RUBI-I) RUBIN M; (SMIK) SMITHKLINE BEECHAM CORP
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001030329	A2	20010503	(200135)*	EN	36
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001010427	A	20010508	(200149)		
US 2002002180	A1	20020103	(200207)		
US 6432966	B1	20020813	(200255)		
EP 1225904	A2	20020731	(200257)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003512421	W	20030402	(200325)		39

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001030329	A2	WO 2000-GB4137	20001027
AU 2001010427	A	AU 2001-10427	20001027
US 2002002180	A1	US 1999-429863	19991029
US 6432966	B1	US 1999-429863	19991029
EP 1225904	A2	EP 2000-971593	20001027
		WO 2000-GB4137	20001027
JP 2003512421	W	WO 2000-GB4137	20001027
		JP 2001-532749	20001027

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001010427	A	Based on	WO 2001030329
EP 1225904	A2	Based on	WO 2001030329
JP 2003512421	W	Based on	WO 2001030329

PRIORITY APPLN. INFO: US 1999-429863 19991029

AB WO 200130329 A UPAB: 20010625
NOVELTY - Use of a combination comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one (lamivudine) (I) or one of its **derivatives** and **BMS-200475** (II) or one of its **derivatives**, in a 200:1-1:1 weight ratio, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a patient pack comprising (I) and (II) and an information insert containing directions on the use of both actives together in combination.
ACTIVITY - Virucide; hepatotropic; antiinflammatory.
MECHANISM OF ACTION - Synergist.
USE - The combination is used to treat hepatitis B virus (HBV) infection resistant to nucleoside and/or non-nucleoside inhibitors of HBV replication (claimed)

ADVANTAGE - (I) exhibits unexpected advantages when used in combination with (II). In particular, the combination shows a statistically significant synergistic anti-HBV effect. Use of this combination may provide synergistic antiviral effects, more complete viral suppression, viral suppression over longer periods, limit the emergence of drug-resistant HBV mutants and allow better management of drug-related toxicities. The use of the drug combination may also result in a decrease in the number of, e.g. tablets administered , thus increasing patient compliance.

Dwg.0/4

ED 20010625

ABEX UPTX: 20010625

ADMINISTRATION - When the combination is in the form of a single pharmaceutical formulation, one or more carriers are present and the formulation is a unit dosage from suitable for oral administration, comprising 25-150 (preferably 100) mg lamivudine and 0.5-20 (preferably 1-5) mg BMS-200475. Otherwise, administration of the actives of the combination can be simultaneous or sequential (all claimed).

EXAMPLE - In a test, the human hepatoblastoma cell line (Hep-G2-2.2.15) which constitutively produces infectious HBV was seeded into 96 well microtiter plates at a density of 5x103 cells per well. These cells were treated with a combination of lamivudine (3TC) and BMS-200475 on triplicate plates. Culture media containing drugs was replenished every other day for 9 days, at which time supernatants were collected and analyzed for HBV content. The lamivudine/BMS-200475 combination was tested three times in triplicate in matrix fashion. The 3 experiments utilized a lamivudine range of 100-0.046 nM (3-fold dilutions in columns). BMS-200475 was serially diluted to form a concentration range of 5.0-0.0002 nM (3.16 fold dilutions in rows). Lamivudine and BMS-200475 were each tested on their respective plates at the same concentrations. Weak but statistically significant synergistic inhibition of HBV replication for the combination of lamivudine and BMS-200475.

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DICTIONARY FILE UPDATES: 17 MAY 2004 HIGHEST RN 682740-60-9

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information enter HELP PROP at an arrow prompt in the file or refer
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http://www.cas.org/ONLINE/DBSS/registryss.html

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FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 14, 2004 (20040514/UP).

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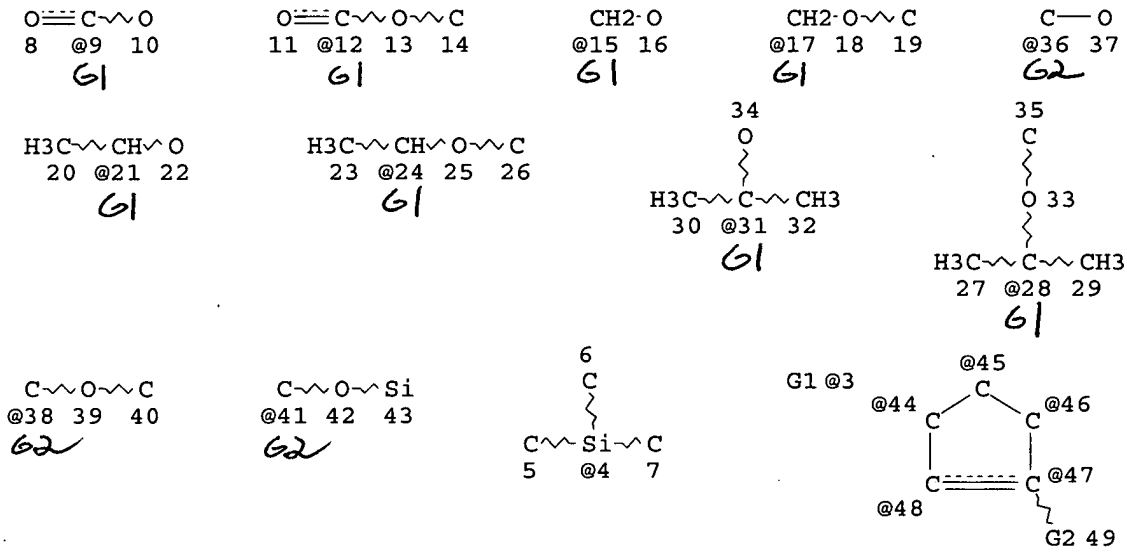
L8 STR



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VAR G2=36/38/41
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VPA 3-48/44/45/46/47 U } variable attachment points
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 10
CONNECT IS E1 RC AT 16
CONNECT IS E1 RC AT 22
CONNECT IS E1 RC AT 34
CONNECT IS E1 RC AT 37 } exactly 1 non-hydrogen connection
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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L23 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

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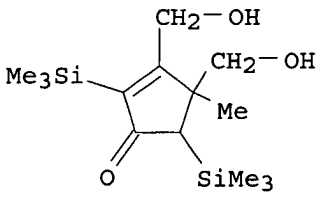
L23 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

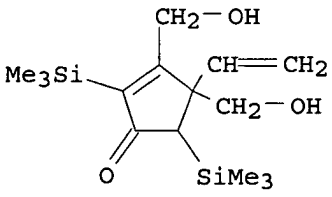
ACCESSION NUMBER: 2003:456472 HCAPLUS
DOCUMENT NUMBER: 139:164535
TITLE: Conjugate Additions of Carbon Nucleophiles to Cyclopentadienones
AUTHOR(S): Pearson, Anthony J.; Kim, Jin Bum
CORPORATE SOURCE: Department of Chemistry, Case Western Reserve University, Cleveland, OH, 44106, USA
SOURCE: Organic Letters (2003), 5(14), 2457-2459
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:164535

IT **575445-38-4P 575445-39-5P 575445-42-0P 575445-43-1P 575445-44-2P 575445-45-3P 575445-46-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of polysubstituted cyclopentenones and cyclopentadienols via 1,4- vs. 1,2-addition of Grignard reagents to cyclopentadienones)

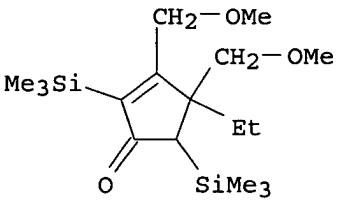
RN 575445-38-4 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(hydroxymethyl)-4-methyl-2,5-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



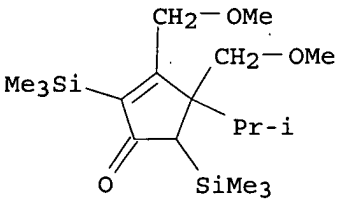
RN 575445-39-5 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethenyl-3,4-bis(hydroxymethyl)-2,5-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



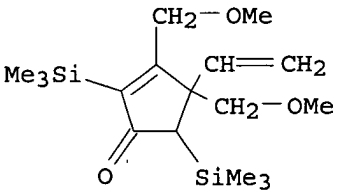
RN 575445-42-0 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethyl-3,4-bis(methoxymethyl)-2,5-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 575445-43-1 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(methoxymethyl)-4-(1-methylethyl)-2,5-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)

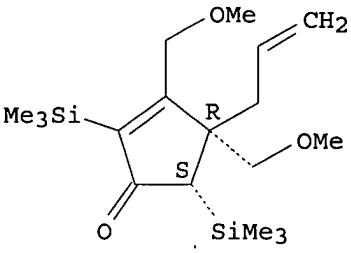


RN 575445-44-2 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethenyl-3,4-bis(methoxymethyl)-2,5-bis(trimethylsilyl)- (9CI) (CA INDEX NAME)



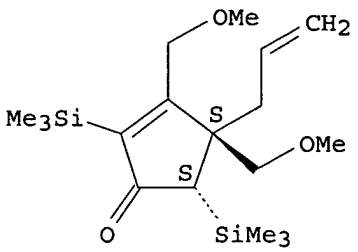
RN 575445-45-3 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(methoxymethyl)-4-(2-propenyl)-2,5-bis(trimethylsilyl)-, (4R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



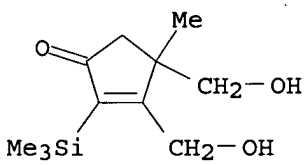
RN 575445-46-4 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(methoxymethyl)-4-(2-propenyl)-2,5-bis(trimethylsilyl)-, (4R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

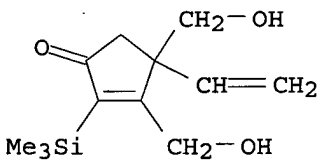


IT **575445-50-0P 575445-51-1P 575445-52-2P**
575445-53-3P 575445-54-4P 575445-55-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of polysubstituted cyclopentenones and cyclopentadienols via 1,4- vs. 1,2-addition of Grignard reagents to cyclopentadienones)

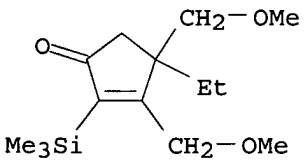
RN 575445-50-0 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(hydroxymethyl)-4-methyl-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



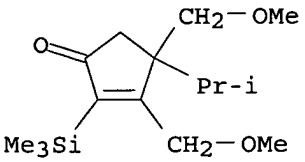
RN 575445-51-1 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethenyl-3,4-bis(hydroxymethyl)-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



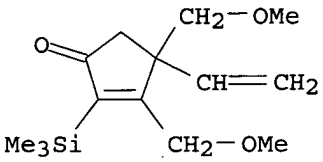
RN 575445-52-2 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethyl-3,4-bis(methoxymethyl)-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



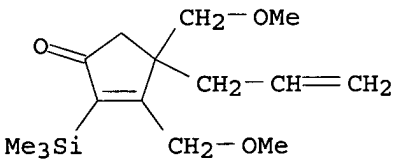
RN 575445-53-3 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(methoxymethyl)-4-(1-methylethyl)-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 575445-54-4 HCAPLUS
CN 2-Cyclopenten-1-one, 4-ethenyl-3,4-bis(methoxymethyl)-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 575445-55-5 HCAPLUS
CN 2-Cyclopenten-1-one, 3,4-bis(methoxymethyl)-4-(2-propenyl)-2-(trimethylsilyl)- (9CI) (CA INDEX NAME)



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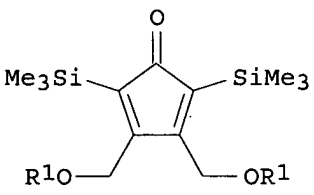

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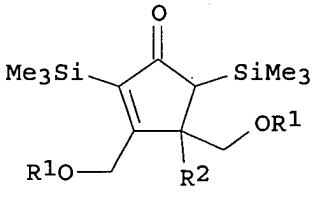
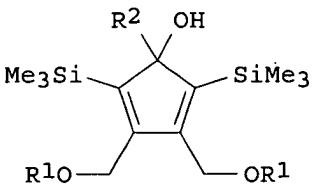


II



III

AB Reactions of cyclopentadienones I (R1 = H, Me) with alkylmagnesium

bromides R2MgBr (R2 = Me, Et, Me2CH, H2C:CH, H2C:CHCH2) gave the corresponding 1,4-adducts II and/or 1,2-adducts III depending on the nature of R1 and R2 substituents.

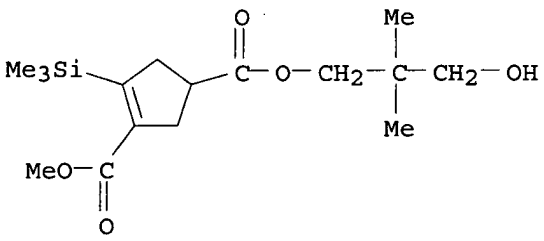
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

=> d l23 ibib hitstr abs 2-
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L23 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:883707 HCAPLUS
DOCUMENT NUMBER: 124:86396
TITLE: A concise synthetic route to cyclopentenes by [3+2] cycloaddition of dipolar trimethylenemethane to alkynes
AUTHOR(S): Yamago, Shigeru; Ejiri, Satoshi; Nakamura, Eiichi
CORPORATE SOURCE: Dep. Chem., Univ. Tokyo, Tokyo, 113, Japan
SOURCE: Angewandte Chemie, International Edition in English (1995), 34(19), 2154-6
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:86396
IT **172538-25-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(a concise synthetic route to cyclopentenes by dipolar cycloaddn. of trimethylenemethane to alkynes)
RN 172538-25-9 HCAPLUS
CN 3-Cyclopentene-1,3-dicarboxylic acid, 4-(trimethylsilyl)-, 1-(3-hydroxy-2,2-dimethylpropyl) 3-methyl ester (9CI) (CA INDEX NAME)



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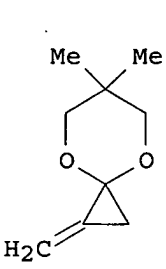
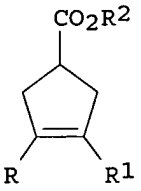
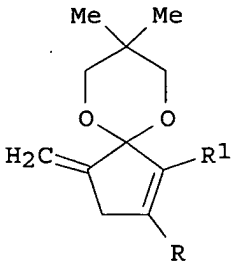


I



II

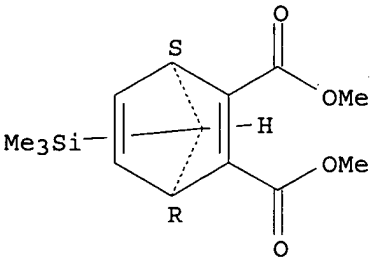


III

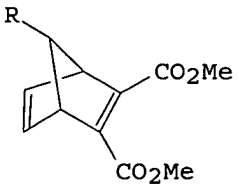
AB Dipolar cycloaddn. of a trimethylenemethane species, generated in situ from methylenecyclopropane I, with alkynes RC.tplbond.CR1 [R = Bu, tetrahydropyranyloxymethyl, SiMe3, Ph, 3,4-methylenedioxyphenyl; R1 = CO2Me, CO2CHMe2, COCHMe2, SO2Me, S(O)Me] leads to cyclopentenecarboxylate esters II (R2 = CH2CMe2CH2OH) in 49-88% yields after ketene acetal hydrolysis. A small amount of exo-methylene isomers III were observed, suggesting the intervention of a single-electron transfer cycloaddn. pathway. The reaction rate increased as the polarity of the solvent was increased: octane < toluene < dimethoxyethane < MeCN < DMSO.

L23 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:558565 HCAPLUS
DOCUMENT NUMBER: 115:158565
TITLE: Synthesis and flash vacuum pyrolysis of dimethyl anti-7-nitro-2,5-norbornadiene-2,3-dicarboxylate
AUTHOR(S): Marchand, Alan P.; Reddy, S. Pulla; Dave, Paritosh R.
CORPORATE SOURCE: Dep. Chem., Univ. North Texas, Denton, TX, 76203-5068, USA
SOURCE: Synthesis (1991), (7), 565-6
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **40467-82-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective nitration of, with nitronium tetrafluoroborate)
RN 40467-82-1 HCAPLUS
CN Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, 7-(trimethylsilyl)-, dimethyl ester, anti- (9CI) (CA INDEX NAME)

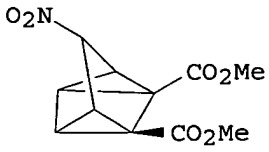
Relative stereochemistry.



GI



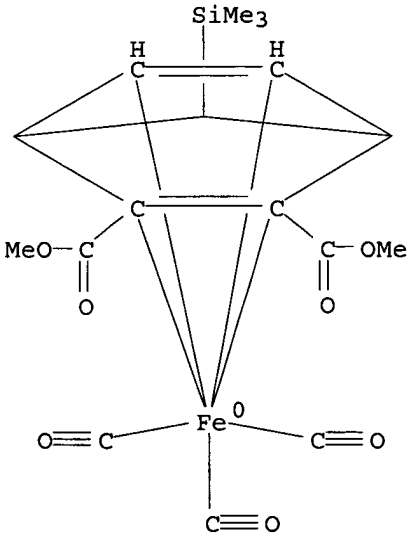
I



III

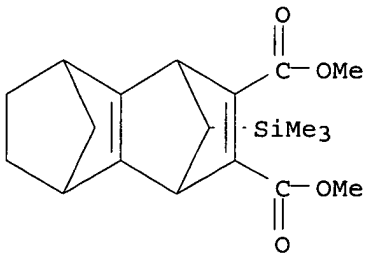
AB Reaction of di-Me anti-7-(trimethylsilyl)-2,5-norbornadiene-2,3-dicarboxylate (I, R = Me3Si) with nitronium tetrafluoroborate affords 65% the title compound (I, R = NO2). Subsequent photolysis of II affords 75% the corresponding substituted quadricyclane derivative III . Flash vacuum pyrolysis of II at 600° affords di-Me phthalate (67%) as the only isolable product.

L23 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:149400 HCAPLUS
DOCUMENT NUMBER: 112:149400
TITLE: Two iron(0) tricarbonyl complexes with substituted norbornadienes
AUTHOR(S): Watson, William H.; Nagl, Ante; Kashyap, Ram P.; Marchand, Alan P.; Dave, Paritosh R.
CORPORATE SOURCE: Dep. Chem., Texas Christ. Univ., Fort Worth, TX, 76129, USA
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1990), C46(1), 24-7
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **125922-39-6**
RL: PRP (Properties)
(crystal structure of)
RN 125922-39-6 HCAPLUS
CN Iron, tricarbonyl[(2,3,5,6-η)-dimethyl 7-(trimethylsilyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate]- (9CI) (CA INDEX NAME)



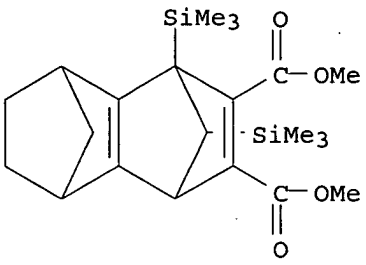
AB Tricarbonyl[2-3;5-6-η-(di-Me 8,9,10-trinorborna-2,5-diene-2,3-dicarboxylato)]iron(0) (I) is monoclinic, space group P21/c, with a 8.274(1), b 7.876(1), c 22.021(2) Å, and β 92.23(1)°; dc = 1.612 for Z = 4. Tricarbonyl[2-3;5-6-η-(di-Me 7-trimethylsilyl-8,9,10-trinorborna-2,5-diene-2,3-dicarboxylato)]iron(0) (II) is orthorhombic, space group P212121, with a 10.738(2), b 12.875(2), and c 14.316(2) Å; dc = 1.410 for Z = 4. The final R's = 0.0417 and 0.0441 for I and II, resp. The Fe in each structure are coordinated to both norbornadiene double bonds, and the geometries involving the 2 double-bond midpoints and the 3 CO groups can be described as distorted trigonal bipyramidal. The 2 double bonds within each norbornadiene moiety are statistically inequivalent with average values of 1.442 and 1.359 Å. The longest bond in each structure is conjugated with the ester groups and occupies an equatorial site. The average distance between Fe(0) and the midpoint of the axial double bond is 2.100 Å, which is significantly longer than the distance to the midpoint of the equatorial double bond of 1.928 Å. The C atoms associated with the longest double bond in each structure are more pyramidalized than those of the short bond.

L23 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1984:6633 HCAPLUS
DOCUMENT NUMBER: 100:6633
TITLE: Silanes in organic synthesis. 20. Regio- and stereochemical definition of silatropic migration within trimethylsilyl-substituted isodicyclopentadienes
AUTHOR(S): Paquette, Leo A.; Charumilind, Pana; Gallucci, Judith C.
CORPORATE SOURCE: Evans Chem. Lab., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Journal of the American Chemical Society (1983), 105(25), 7364-75
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 100:6633
IT **87556-06-7P 87556-23-8P 87585-18-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and epoxidn. of)
RN 87556-06-7 HCAPLUS
CN 1,4:5,8-Dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-10-(trimethylsilyl)-, dimethyl ester, stereoisomer (9CI) (CA INDEX NAME)

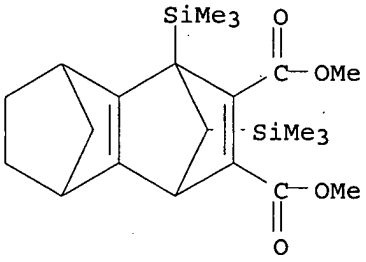


RN 87556-23-8 HCAPLUS
CN 1,4:5,8-Dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1,10-bis(trimethylsilyl)-, dimethyl ester, (1α,4β,5β,8.bet

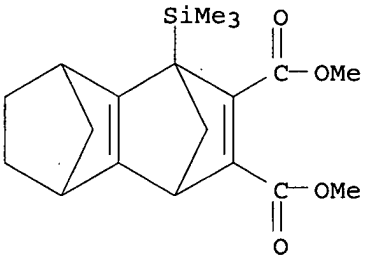
a.,10R*)- (9CI) (CA INDEX NAME)



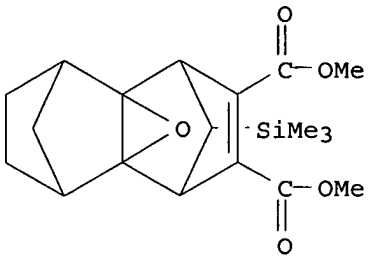
RN 87585-18-0 HCAPLUS
CN 1,4:5,8-Dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1,10-bis(trimethylsilyl)-, dimethyl ester, (1α,4β,5α,8.alpha.,10R*)- (9CI) (CA INDEX NAME)



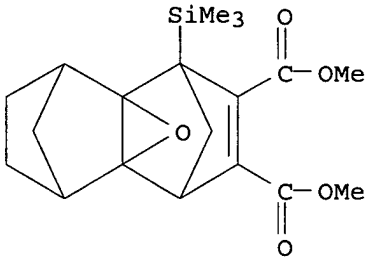
IT **87556-12-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peracid oxidation of)
RN 87556-12-5 HCAPLUS
CN 1,4:5,8-Dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1-(trimethylsilyl)-, dimethyl ester, (1α,4β,5β,8β)- (9CI) (CA INDEX NAME)



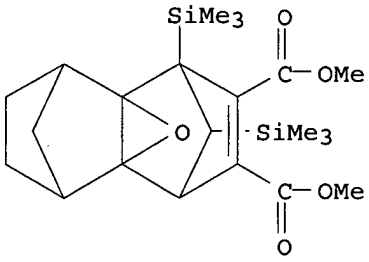
IT **87556-07-8P 87556-13-6P 87556-24-9P**
87585-19-1P 87678-00-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 87556-07-8 HCAPLUS
CN 4a,8a-Epoxy-1,4:5,8-dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-11-(trimethylsilyl)-, dimethyl ester, stereoisomer (9CI) (CA INDEX NAME)



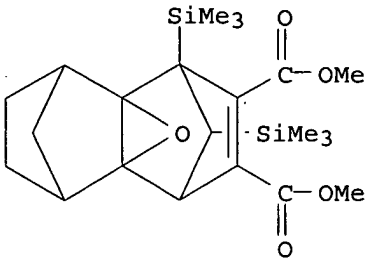
RN 87556-13-6 HCAPLUS
CN 4a,8a-Epoxy-1,4:5,8-dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1-(trimethylsilyl)-, dimethyl ester, (1α,4β,4aβ,5β,8β,8aβ)- (9CI) (CA INDEX NAME)



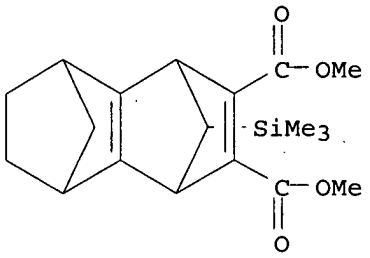
RN 87556-24-9 HCAPLUS
CN 4a,8a-Epoxy-1,4:5,8-dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1,11-bis(trimethylsilyl)-, dimethyl ester, (1α,4β,4aβ,5β,8β,8aβ,11S*)- (9CI) (CA INDEX NAME)



RN 87585-19-1 HCAPLUS
CN 4a,8a-Epoxy-1,4:5,8-dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-1,11-bis(trimethylsilyl)-, dimethyl ester, (1α,4α,4aα,5β,8β,8aα,11S*)- (9CI) (CA INDEX NAME)



RN 87678-00-0 HCAPLUS
CN 1,4:5,8-Dimethanonaphthalene-2,3-dicarboxylic acid, 1,4,5,6,7,8-hexahydro-10-(trimethylsilyl)-, dimethyl ester, (1α,4α,5α,8α,10R*)- (9CI) (CA INDEX NAME)



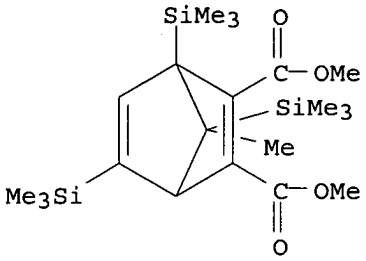
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Reaction of the anion of isodicyclopentadiene with Me3SiCl proceeds with predominant below-plane capture of the electrophile (I/II = 91:9) as expected from long-range stereoelectronic control. To make exo isomer II accessible in quantity, this product was deprotonated to generate an ion where added electronic interactions with the Me3Si substituent leads to more stereorandom protonation (I/II = 54:46). Alternatively, silylation of this intermediate gave III. The course of various Diels-Alder cycloaddns. to I-III has been examined with a view to gaining insight into possible silatropic migrations within these systems. Whereas the reactions involving II occurred exclusively from the endo direction without evidence of silatropic migration, those involving I were more varied. Thus, N-phenylmaleimide captured only the [1,5].apprx.Si migrated isomer IV to give V. Because MeO2CC.tplbond.CCO2Me is sterically inhibited from adding to such isomerized dienes, direct addition to I occurs in this instance exclusively from the exo direction. Preequilibration of I at 140° provides a still wider array of cycloadducts. With BF3 catalysis, desilylation occurs. N-Methyltriazolinedione and (NC)2C:C(CN)2 react with I by an ene mechanism, the first with retention of the silyl group. In the case of III, Diels-Alder reaction proceeds via either VI or the [1,5].apprx.Si/[1,5].apprx.H isomers VII and VIII. That sigmatropic migration can advance as far as IX was demonstrated by independent thermolysis expts. The crystal structures of X and XI were determined

L23 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1975:577910 HCAPLUS
DOCUMENT NUMBER: 83:177910
TITLE: Intramolecular rearrangements in tris(trimethylsilyl)cyclopentadiene
AUTHOR(S): Ustynyuk, Yu. A.; Luzikov, Yu. N.; Mstislavskii, V. I.; Azizov, A. A.; Pribytkova, I. M.
CORPORATE SOURCE: Chem. Dep., M. V. Lomonosov State Univ., Moscow, USSR
SOURCE: Journal of Organometallic Chemistry (1975), 96(3), 335-53
CODEN: JORCAI; ISSN: 0022-328X
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **57377-15-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 57377-15-8 HCAPLUS
CN Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, 7-methyl-1,5,7-tris(trimethylsilyl)-, dimethyl ester (9CI) (CA INDEX NAME)

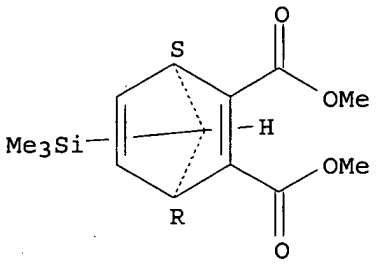


AB Temperature dependences of line shapes and line intensities in NMR spectra recorded for 2,5,5-tris(trimethylsilyl)cyclopentadiene (I) and for the deuterated analog (II) demonstrate that metallotropic and prototropic intramol. rearrangements occur in these compds. Four possible migration routes for metallotropic rearrangements in I and II are considered. Temperature dependences of PMR and 13C-{1H} NMR spectra for I and II and a Diels-Alder reaction of I with acetylenedicarboxylic ester are explained only in terms of four successive 1,2 shifts of the metal. A detailed description of dynamic processes in I is made on the basis of total line shape studies carried out for 1H-{2H} NMR spectra of II under exchange conditions. The effect of introduction of organometallic groups in the cyclopentadienyl ring on the metallotropic rearrangement is discussed. An attempt is made to extend the concept of relative migratory ability of metals to include cyclopentadienyl ligands.

L23 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1973:43631 HCAPLUS
DOCUMENT NUMBER: 78:43631
TITLE: Cyclopentadienylsilanes and germanes. Influence of the heteroatom and its substituents on the cycloaddition to acetylenic dienophiles
AUTHOR(S): Laporterie, Andre; Dubac, Jacques; Mazerolles, Pierre
CORPORATE SOURCE: Lab. Organomet., Univ. Paul Sabatier, Toulouse, Fr.
SOURCE: Journal of Organometallic Chemistry (1972), 46(1), C3-C6
CODEN: JORCAI; ISSN: 0022-328X
DOCUMENT TYPE: Journal
LANGUAGE: French

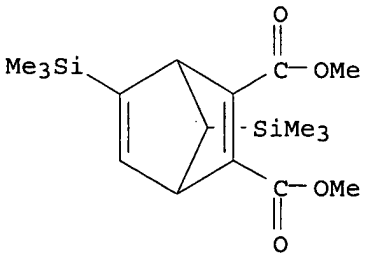
IT **40467-82-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 40467-82-1 HCAPLUS
CN Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, 7-(trimethylsilyl)-, dimethyl ester, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



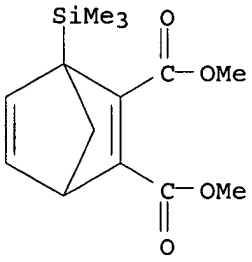
AB The isomers resulting from H migration in various silyl-and germylcyclopentadienes are isolated by a Diels-Alder reaction with ethynyltrichlorogermane. The ratio of the isomeric adducts formed is determined both by the heteroatom of the diene and by the alkyl or halogen substituent bonded to the heteroatom.

L23 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:513287 HCAPLUS
DOCUMENT NUMBER: 77:113287
TITLE: Nuclear magnetic resonance spectroscopy of metal cyclopentadienyls. X. Proton magnetic resonance spectra of, and dynamic behavior in, bis(trimethylsilyl)cyclopentadiene
AUTHOR(S): Ustynyuk, Yu. A.; Kisin, A. V.; Pribytkova, I. M.; Zenkin, A. A.; Antonova, N. D.
CORPORATE SOURCE: Chem. Dep., M. V. Lomonosov State Univ., Moscow, USSR
SOURCE: Journal of Organometallic Chemistry (1972), 42(1), 47-63
CODEN: JORCAI; ISSN: 0022-328X
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **39031-54-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 39031-54-4 HCAPLUS
CN Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid, 5,7-bis(trimethylsilyl)-, dimethyl ester (9CI) (CA INDEX NAME)



AB The PMR spectra of bis(trimethylsilyl)cyclopentadiene (I) were studied at -30° to +220° indicating that I is a mixture of the 5,5-(Ia), 2,5-(Ib), 1,4-(Ic), and 1,3-(Id) isomers, the ratio being 132/3.6/2.2/1 at -30°. The structures were proved using INDOR and spin-decoupling techniques and through Diels-Alder reactions with dienophiles or metallation with an aminostannane. Ib exhibits a degenerate metallotropic rearrangement which proceeds via the 1,2 shift of the 5-positioned Me3Si group (Ea 14.5 ± 1.8 kcal/mole, ΔS≠ -1.5 ± 4 e.u.). The interconversion of Ia and Ib proceeds via the 1,3 shift of the Me3Si group. The methyl chemical shifts were processed using a MINIMAX 1 program to yield the thermodynamic characteristics of the Ia .dblarw. Ib metallotropic tautomeric equilibrium, i.e., ΔH 2.73 kcal/mole and ΔS 4.99 e.u. The values of the activation parameters were obtained for the metallotropic rearrangement of Ib into Ia (Ea 15.8 ± 1.0 kcal/mole, ΔS≠ -4.7 ± 4 e.u.) and Ia into Ib (Ea 18.6 ± 1.0 kcal/mole, ΔS≠ 0.3 ± 4 e.u.). Above + 120° Ic .dblarw. Ib .dblarw. Id hydrogen migration was observed, the process being fast relative to the NMR time scale. The activation energy was estimated as 21 kcal/mole for the rearrangement of Ic to Ib.

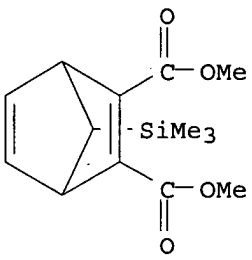
L23 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1970:120763 HCAPLUS
DOCUMENT NUMBER: 72:120763
TITLE: Hydrogen and trimethylsilyl migrations in 5-(trimethylsilyl) cyclopentadiene
AUTHOR(S): Ashe, Arthur J., III
CORPORATE SOURCE: Dep. of Chem., Univ. of Michigan, Ann Arbor, MI, USA
SOURCE: Journal of the American Chemical Society (1970), 92(5), 1233-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **28123-38-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 28123-38-8 HCAPLUS
CN 2,5-Norbornadiene-2,3-dicarboxylic acid, 1-(trimethylsilyl)-, dimethyl ester (8CI) (CA INDEX NAME)



AB 5-Trimethylsilyl, 1-trimethylsilyl-, and 2-trimethylsilylcyclopentadiene were identified by NMR spectroscopy and formation of adducts with dimethyl acetylenedicarboxylate. The rate of H migration of 5-trimethylsilylcyclopentadiene is 2.0 + 1013 exp(-26.2 kcal mole-1/RT). This is 106 slower than trimethylsilyl migration.

L23 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:505546 HCAPLUS
DOCUMENT NUMBER: 69:105546

TITLE: Ethynylsilanes. IV. The effect of temperature on the Diels-Alder addition of acetylenic dienophiles to 1-trimethylsilylcyclopentadiene
AUTHOR(S): Kraihanzel, Charles S.; Losee, M. L.
CORPORATE SOURCE: Lehigh Univ., Bethlehem, PA, USA
SOURCE: Journal of the American Chemical Society (1968), 90(17), 4701-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **21410-42-4**
RL: PRP (Properties)
(nuclear magnetic resonance of)
RN 21410-42-4 HCAPLUS
CN 2,5-Norbornadiene-2,3-dicarboxylic acid, 7-(trimethylsilyl)-, dimethyl ester (8CI) (CA INDEX NAME)



AB Dimethyl acetylenedicarboxylate was treated with 1-trimethylsilylcyclopentadiene to yield a mixture of 7-trimethylsilyl- and 5-trimethylsilyl-2,3-bis(methoxycarbonyl)-bicyclo[2.2.1]heptadienes. Thermal isomerization of the 7-trimethylsilyl derivative to the 5-trimethylsilyl isomer did not occur. Reactions between Me3SiC.tplbond.CR, (R = H, Ac, or CO2Et), and 1-trimethylsilylcyclopentadiene were carried out at 180-260°, and only vinyl-substituted derivs. were obtained. It is suggested that 1-trimethylsilylcyclopentadiene undergoes temperature-dependent tautomerism, which may be viewed as a 1,3-proton shift, to form 3-trimethylsilylcyclopentadiene. The reactions between the various dienophiles and this tautomeric form of the diene would be expected to yield the products observed at the high temperature

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